



Clinical trial results:

A phase II, double-blind, multicentre study to evaluate the safety and immunogenicity of a booster dose of new formulations of GlaxoSmithKline Biologicals' combined DTPa-HBV-IPV/Hib vaccine in healthy toddlers, previously primed with three doses of the same vaccine in study 113948 (DTPA-HBV-IPV-124 PRI).

Summary

EudraCT number	2011-000876-33
Trial protocol	FI Outside EU/EEA
Global end of trial date	08 August 2013

Results information

Result version number	v1
This version publication date	02 May 2016
First version publication date	01 February 2015

Trial information

Trial identification

Sponsor protocol code	114843
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01453998
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 November 2012
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the immunogenicity of at least one DTPa-HBV-IPV/Hib formulation is non-inferior to the licensed formulation in terms of seroprotection rates to diphtheria, tetanus, hepatitis B, poliovirus types 1, 2 and 3 and PRP antigens and in terms of antibody geometric mean concentrations (GMCs) for pertussis antigens one month after the booster dose.

Protection of trial subjects:

As with all injectable vaccines, appropriate medical treatment was always readily available in case of anaphylactic reactions following the administration of the vaccine.
For this reason, the vaccinee remained under medical supervision for 30 minutes after vaccination.
DTPa vaccination was administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may have occurred following an intramuscular administration to these subjects.
DTPa vaccination was under no circumstances administered intravenously.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 October 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Dominican Republic: 248
Country: Number of subjects enrolled	Finland: 409
Worldwide total number of subjects	657
EEA total number of subjects	409

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	657
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 272 subjects were enrolled in the study before the second protocol amendment and total of 385 after the amendment. After amendment 2, all subjects yet to receive a booster dose of a GSK217744 formulation, were administered the Infanrix hexa™ vaccine.

Pre-assignment

Screening details:

A total of 272 subjects were enrolled in the study before the second protocol amendment and total of 385 after the amendment. After amendment 2, all subjects yet to receive a booster dose of a GSK217744 formulation, were administered the Infanrix hexa™ vaccine.

Period 1

Period 1 title	Before Protocol Amendment 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK217744 Group 1

Arm description:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation A vaccine in the primary study and a booster dose of either GSK217744 formulation A vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation A vaccine in the primary study and a booster dose of either GSK217744 formulation A vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Investigational medicinal product name	Biological: GSK217744
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation A vaccine in the primary study and a booster dose of either GSK217744 formulation A vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively

Arm title	GSK217744 Group 2
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Arm description:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation B vaccine in the primary study and a booster dose of either GSK217744 formulation B vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation B vaccine in the primary study and a booster dose of either GSK217744 formulation B vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Investigational medicinal product name	GSK217744
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation B vaccine in the primary study and a booster dose of either GSK217744 formulation B vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Arm title	Infanrix hexa Group
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Arm description:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the Infanrix hexa™ vaccine in the primary study and a booster dose of Infanrix hexa™ in this study, co-administered with a booster dose of Prevenar 13®. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Arm type	Experimental
Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the Infanrix hexa™ vaccine in the primary study and a booster dose of Infanrix hexa™ in this study, co-administered with a booster dose of Prevenar 13®. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the Infanrix hexa™ vaccine in the primary study and a booster dose of Infanrix hexa™ in this study, co-administered with a booster dose of Prevenar 13®. The Infanrix hexa™ and Prevenar 13® vaccines

were administered intramuscularly into the right and left sides of the thigh, respectively.

Number of subjects in period 1	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Started	85	88	99
Completed	85	88	99

Period 2

Period 2 title	After Protocol Amendment 2
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	GSK217744 Group 1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	infanrix hexa™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, licensed formulation, intramuscular into right

Investigational medicinal product name	Prevenar 13®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single co-administered dose, intramuscular into left thigh

Investigational medicinal product name	GSK217744
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection

Routes of administration	Intramuscular use
Dosage and administration details:	
Single dose, licensed formulation, intramuscular into right	

Arm title	GSK217744 Group 2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
Single dose, licensed formulation, intramuscular into right

Arm title	Infanrix hexa Group
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
Single dose, licensed formulation, intramuscular into right

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: More subjects were enrolled in period 2 therefore it was considered the baseline period.

Number of subjects in period 2	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Started	103	99	183
Completed	102	99	183
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Baseline characteristics

Reporting groups^[1]

Reporting group title	GSK217744 Group 1
Reporting group description: -	
Reporting group title	GSK217744 Group 2
Reporting group description: -	
Reporting group title	Infanrix hexa Group
Reporting group description: -	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: More subjects were enrolled in period 2 therefore it was considered the baseline period.

Reporting group values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Number of subjects	103	99	183
Age categorical			
Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
Units: months			
arithmetic mean	14	14	14
standard deviation	± 0.5	± 0.46	± 0.72
Gender categorical			
Units: Subjects			
Female	47	54	89
Male	56	45	94

Reporting group values	Total		
Number of subjects	385		
Age categorical			
Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			

85 years and over			
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Age continuous Units: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	190		
Male	195		

End points

End points reporting groups

Reporting group title	GSK217744 Group 1
Reporting group description: Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation A vaccine in the primary study and a booster dose of either GSK217744 formulation A vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.	
Reporting group title	GSK217744 Group 2
Reporting group description: Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation B vaccine in the primary study and a booster dose of either GSK217744 formulation B vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.	
Reporting group title	Infanrix hexa Group
Reporting group description: Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the Infanrix hexa™ vaccine in the primary study and a booster dose of Infanrix hexa™ in this study, co-administered with a booster dose of Prevenar 13®. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.	
Reporting group title	GSK217744 Group 1
Reporting group description: -	
Reporting group title	GSK217744 Group 2
Reporting group description: -	
Reporting group title	Infanrix hexa Group
Reporting group description: -	

Primary: Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies. ^[1]
End point description: A seroprotected subject was defined as a vaccinated subject who had anti-D and anti-T antibody concentrations ≥ 0.1 international units per milliliter (IU/mL).	
End point type	Primary
End point timeframe: Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled before protocol amendment 2)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	82	90	
Units: Subjects				
Anti-D PRE [N=81;82;89]	78	80	84	
Anti-D POST [N=81;82;90]	81	82	90	
Anti-T PRE [N=81;82;89]	76	78	85	
Anti-T POST [N=81;82;90]	81	82	90	

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point title	Concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies. ^[2]
End point description: Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.1 IU/mL.	
End point type	Primary
End point timeframe: Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled before protocol amendment 2)	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	82	90	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D PRE [N=81;82;89]	0.357 (0.305 to 0.419)	0.445 (0.381 to 0.52)	0.401 (0.343 to 0.468)	
Anti-D POST [N=81;82;90]	5.652 (4.985 to 6.408)	5.494 (4.891 to 6.171)	6.772 (5.897 to 7.777)	
Anti-T PRE [N=81;82;89]	0.358 (0.301 to 0.427)	0.362 (0.306 to 0.428)	0.394 (0.337 to 0.459)	
Anti-T POST [N=81;82;90]	5.015 (4.341 to 5.794)	5.034 (4.366 to 5.803)	5.571 (4.869 to 6.374)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-polyribosyl-ribitol phosphate (anti-PRP)

End point title	Number of seroprotected subjects for anti-polyribosyl-ribitol phosphate (anti-PRP) ^[3]
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End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-PRP antibody concentrations ≥ 0.15 micrograms per milliliter ($\mu\text{g/mL}$).

End point type	Primary
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End point timeframe:

Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled before protocol amendment 2)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	82	90	
Units: Subjects				
Anti-PRP PRE [N=81;82;89]	41	45	52	
Anti-PRP POST [N=81;82;90]	81	82	90	

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-PRP antibodies

End point title	Concentrations for anti-PRP antibodies ^[4]
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End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was $0.15 \mu\text{g/mL}$.

End point type	Primary
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End point timeframe:

Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled before protocol amendment 2)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	82	90	
Units: Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP PRE [N=81;82;89]	0.173 (0.138 to 0.216)	0.175 (0.142 to 0.216)	0.236 (0.182 to 0.307)	

Anti-PRP POST [N=81;82;90]	12.765 (9.3 to 17.52)	15.904 (11.723 to 21.576)	17.099 (12.966 to 22.55)	
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Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies ^[5]
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End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-D and anti-T antibody concentrations ≥ 0.1 international units per milliliter (IU/mL).

End point type	Primary
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End point timeframe:

Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled after protocol amendment 2)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	95	173	
Units: Subjects				
Anti-D PRE [N=96;95;170]	84	83	159	
Anti-D POST [N=96;95;173]	96	95	173	
Anti-T PRE [N=96;95;170]	87	87	167	
Anti-T POST [N=96;95;173]	96	95	173	

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies

End point title	Concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies ^[6]
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End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.1 IU/mL.

End point type	Primary
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End point timeframe:

Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled after protocol amendment 2)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	95	173	
Units: Units:IU/mL				
geometric mean (confidence interval 95%)				
Anti-D PRE [N=96;95;170]	0.26 (0.217 to 0.311)	0.245 (0.206 to 0.292)	0.306 (0.272 to 0.343)	
Anti-D POST [N=96;95;173]	6.224 (5.411 to 7.159)	6.549 (5.781 to 7.418)	6.105 (5.641 to 6.607)	
Anti-T PRE [N=96;95;170]	0.309 (0.259 to 0.369)	0.306 (0.255 to 0.367)	0.384 (0.346 to 0.425)	
Anti-T POST [N=96;95;173]	5.713 (4.923 to 6.629)	5.895 (5.01 to 6.937)	5.649 (5.074 to 6.289)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroprotected subjects for anti-polyribosyl-ribitol phosphate (anti-PRP).

End point title	Number of seroprotected subjects for anti-polyribosyl-ribitol phosphate (anti-PRP). ^[7]
End point description:	A seroprotected subject was defined as a vaccinated subject who had anti-PRP antibody concentrations ≥ 0.15 micrograms per milliliter ($\mu\text{g/mL}$).
End point type	Primary
End point timeframe:	Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled after protocol amendment 2)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	95	173	
Units: Subjects				
Anti-PRP PRE [N=96;95;170]	70	70	111	
Anti-PRP POST [N=96;95;173]	96	95	171	

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations for anti-PRP antibodies.

End point title	Concentrations for anti-PRP antibodies. ^[8]
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End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection cut-off of the assay was 0.15 µg /mL.

End point type	Primary
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End point timeframe:

Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled after protocol amendment 2)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	95	173	
Units: Units:µg /mL				
geometric mean (confidence interval 95%)				
Anti-PRP PRE [N=96;95;170]	0.357 (0.269 to 0.474)	0.359 (0.271 to 0.475)	0.273 (0.224 to 0.332)	
Anti-PRP POST [N=96;95;173]	17.459 (12.846 to 23.727)	18.576 (13.845 to 24.923)	18.04 (14.522 to 22.41)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes.

End point title	Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes.
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End point description:

A seropositive subject was defined as a vaccinated subject who had anti- pneumococcal antibody concentrations ≥ 0.15 micrograms per milliliter (µg/mL). The anti-PNE serotypes assessed were 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

End point type	Secondary
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End point timeframe:

1 month post booster vaccination (POST) (subjects enrolled before protocol amendment 2)

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	53	
Units: Subjects				
Anti- PNE 1 [N=50;50;53]	50	50	53	
Anti- PNE 3 [N=40;44;44]	40	43	43	
Anti- PNE 4 [N=50;50;53]	50	50	53	
Anti- PNE 5 [N=50;50;53]	50	50	53	
Anti- PNE 6A [N=50;50;53]	50	50	53	
Anti- PNE 6B [N=50;50;53]	50	49	53	
Anti- PNE 7F [N=50;50;53]	50	50	53	
Anti- PNE 9V [N=50;50;53]	50	50	53	
Anti- PNE 14 [N=50;50;53]	49	50	53	
Anti- PNE 18C [N=50;50;53]	49	50	53	
Anti- PNE 19A [N=49;50;53]	49	50	53	
Anti- PNE 19F [N=50;50;53]	50	50	53	
Anti- PNE 23F [N=50;47;52]	50	47	52	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PNE antibodies.

End point title	Concentrations for anti-PNE antibodies.
End point description:	
Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity cut-off of the assay was 0.15 µg /mL. The anti-PNE serotypes assessed were 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.	
End point type	Secondary
End point timeframe:	
Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled before protocol amendment 2)	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	50	
Units: Units:µg /mL				
geometric mean (confidence interval 95%)				
Anti- PNE 1 [N=50;50;53]	2.07 (1.69 to 2.53)	2.16 (1.75 to 2.68)	2.27 (1.84 to 2.8)	
Anti- PNE 3 [N=40;44;44]	0.76 (0.62 to 0.93)	0.87 (0.66 to 1.15)	0.88 (0.69 to 1.14)	
Anti- PNE 4 [N=50;50;53]	1.87 (1.51 to 2.32)	1.83 (1.46 to 2.28)	2.14 (1.72 to 2.66)	
Anti- PNE 5 [N=50;50;53]	1.18 (0.97 to 1.42)	1.1 (0.92 to 1.33)	1.21 (0.99 to 1.49)	

Anti- PNE 6A [N=50;50;53]	7.71 (6.49 to 9.16)	6.92 (5.53 to 8.64)	8.63 (6.79 to 10.96)	
Anti- PNE 6B [N=50;50;53]	4.24 (3.39 to 5.3)	4.21 (3.17 to 5.59)	4.58 (3.45 to 6.08)	
Anti- PNE 7F [N=50;50;53]	3.27 (2.75 to 3.89)	3.42 (2.94 to 3.97)	4.27 (3.58 to 5.08)	
Anti- PNE 9V [N=50;50;53]	1.68 (1.33 to 2.11)	1.52 (1.25 to 1.85)	1.63 (1.29 to 2.06)	
Anti- PNE 14 [N=50;50;53]	8.22 (6.27 to 10.77)	8.8 (7.01 to 11.06)	8.97 (7.29 to 11.02)	
Anti- PNE 18C [N=50;50;53]	1.5 (1.13 to 1.99)	1.63 (1.32 to 2.01)	1.64 (1.33 to 2.02)	
Anti- PNE 19A [N=49;50;53]	7 (5.76 to 8.51)	8.05 (6.39 to 10.13)	6.7 (5.14 to 8.73)	
Anti- PNE 19F [N=50;50;53]	7.15 (5.86 to 8.74)	7.34 (5.89 to 9.15)	6.72 (5.32 to 8.48)	
Anti- PNE 23F [N=50;47;52]	3.74 (2.87 to 4.88)	4.54 (3.67 to 5.63)	3.94 (2.97 to 5.23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes

End point title	Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes
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End point description:

A seropositive subject was defined as a vaccinated subject who had anti- pneumococcal antibody concentrations ≥ 0.15 micrograms per milliliter ($\mu\text{g/mL}$). The anti-PNE serotypes assessed were 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

End point type	Secondary
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End point timeframe:

1 month post booster vaccination (POST) (subjects enrolled after protocol amendment 2)

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	9	46	
Units: Subjects				
Anti- PNE 1 [N=9;9;46]	9	9	46	
Anti- PNE 3 [N=8;8;39]	8	8	39	
Anti- PNE 4 [N=9;9;46]	9	9	46	
Anti- PNE 5 [N=9;9;46]	9	9	46	
Anti- PNE 6A [N=9;9;46]	9	9	46	
Anti- PNE 6B [N=9;9;46]	9	9	46	
Anti- PNE 7F [N=9;9;46]	9	9	46	
Anti- PNE 9V [N=9;9;46]	9	9	46	
Anti- PNE 14 [N=9;9;46]	9	9	46	
Anti- PNE 18C [N=9;9;46]	9	9	46	
Anti- PNE 19A [N=9;8;46]	9	9	46	

Anti- PNE 19F [N=9;9;46]	9	9	46	
Anti- PNE 23F [N=9;9;46]	9	9	46	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PNE antibodies.

End point title	Concentrations for anti-PNE antibodies.
End point description:	
Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity cut-off of the assay was 0.15 µg /mL. The anti-PNE serotypes assessed were 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.	
End point type	Secondary
End point timeframe:	
Before (PRE) and 1 month post booster vaccination (POST) (subjects enrolled after protocol amendment 2)	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	9	46	
Units: Units:µg /mL				
geometric mean (confidence interval 95%)				
Anti- PNE 1 [N=9;9;46]	2.58 (1.11 to 6.03)	2.92 (2.08 to 4.1)	2.79 (2.24 to 3.48)	
Anti- PNE 3 [N=8;8;39]	0.95 (0.45 to 1.99)	0.98 (0.68 to 1.4)	0.77 (0.65 to 0.92)	
Anti- PNE 4 [N=9;9;46]	2.74 (1.18 to 6.38)	1.85 (1.26 to 2.71)	2.19 (1.78 to 2.7)	
Anti- PNE 5 [N=9;9;46]	1.49 (0.75 to 2.94)	1.14 (0.72 to 1.8)	1.25 (1.05 to 1.48)	
Anti- PNE 6A [N=9;9;46]	11.76 (6.26 to 22.09)	6.92 (4.43 to 10.83)	8.38 (6.73 to 10.42)	
Anti- PNE 6B [N=9;9;46]	6.4 (2.14 to 19.16)	5.84 (2.97 to 11.49)	5.02 (4 to 6.31)	
Anti- PNE 7F [N=9;9;46]	8.04 (4.56 to 14.16)	3.74 (2.38 to 5.86)	3.86 (3.26 to 4.57)	
Anti- PNE 9V [N=9;9;46]	1.96 (1.07 to 3.58)	1.87 (1.14 to 3.08)	1.77 (1.42 to 2.21)	
Anti- PNE 14 [N=9;9;46]	9.88 (5.23 to 18.67)	6.78 (3.97 to 11.56)	8.23 (6.67 to 10.16)	
Anti- PNE 18C [N=9;9;46]	2.95 (1.42 to 6.11)	1.52 (1.17 to 1.99)	1.67 (1.34 to 2.07)	
Anti- PNE 19A [N=9;8;46]	6.48 (3.08 to 13.61)	12.89 (6.08 to 27.32)	7.56 (6.06 to 9.44)	
Anti- PNE 19F [N=9;9;46]	5.48 (2.29 to 13.1)	5.97 (2.93 to 12.16)	7.42 (5.78 to 9.54)	
Anti- PNE 23F [N=9;9;46]	6.26 (2.67 to 14.66)	6.4 (4.8 to 8.53)	4.53 (3.68 to 5.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms.

End point title	Number of subjects reporting any solicited local symptoms.
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End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any local symptom regardless of intensity grade.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period. (subjects enrolled before protocol amendment 2)

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	88	99	
Units: Subjects				
Any pain	56	67	63	
Any redness	55	56	59	
Any swelling	45	43	48	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms.

End point title	Number of subjects reporting any solicited general symptoms.
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End point description:

Solicited local symptoms assessed were drowsiness, irritability/fussiness, loss of appetite and fever [axillary temperature above (\geq) 37.5 degrees Celsius ($^{\circ}$ C)]. Any = occurrence of any local symptom regardless of intensity grade.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period. (subjects enrolled before protocol amendment 2)

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	88	99	
Units: Subjects				
Any drowsiness	54	47	47	
Any irritability/fussiness	69	73	74	
Any loss of appetite	43	45	46	
Any fever	37	41	37	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).
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End point description:

An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any = occurrence of an AE regardless of intensity grade or relationship to study vaccination.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) follow up period after vaccination. (subjects enrolled before protocol amendment 2)

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	88	99	
Units: Subjects				
Any AEs [Units:Subjects]	42	39	67	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs).

End point title	Number of subjects reporting any serious adverse events (SAEs).
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End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. Any SAE = any SAE regardless of assessment of relationship to study vaccination.

End point type	Secondary
End point timeframe:	
During the entire study period (Days 0-30). (subjects enrolled before protocol amendment 2)	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	88	99	
Units: Subjects				
Any SAEs [Units:Subjects]	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms

End point title	Number of subjects reporting any solicited local symptoms
End point description:	
Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any local symptom regardless of intensity grade.	
End point type	Secondary
End point timeframe:	
During the 4-day (Days 0-3) post-vaccination period. (subjects enrolled after protocol amendment 2)	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	99	183	
Units: Subjects				
Any pain	51	57	98	
Any redness	24	26	73	
Any swelling	29	28	58	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms

End point title	Number of subjects reporting any solicited general symptoms
End point description:	
Solicited local symptoms assessed were drowsiness, irritability/fussiness, loss of appetite and fever [axillary temperature above (\geq) 37.5 degrees Celsius ($^{\circ}$ C)]. Any = occurrence of any local symptom	

regardless of intensity grade.

End point type	Secondary
End point timeframe:	
During the 4-day (Days 0-3) post-vaccination period. (subjects enrolled after protocol amendment 2)	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	99	183	
Units: Subjects				
Any drowsiness	30	35	67	
Any irritability/fussiness	37	47	102	
Any loss of appetite	27	28	58	
Any fever	37	40	83	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs)

End point title	Number of subjects reporting any unsolicited adverse events (AEs)
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End point description:

An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any = occurrence of an AE regardless of intensity grade or relationship to study vaccination.

End point type	Secondary
End point timeframe:	
Within the 31-day (Days 0-30) follow up period after vaccination. (subjects enrolled after protocol amendment 2)	

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	99	183	
Units: Subjects				
Any AEs [Units:Subjects]	26	24	46	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs)

End point title	Number of subjects reporting any serious adverse events (SAEs)
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End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. Any SAE = any SAE regardless of assessment of relationship to study vaccination.

End point type	Secondary
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End point timeframe:

During the entire study period (Days 0-30). (subjects enrolled after protocol amendment 2)

End point values	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	103	99	183	
Units: Subjects				
Any SAEs [Units:Subjects]	1	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 4-day follow-up period after vaccination; unsolicited AEs: 31-day follow-up period after vaccination; SAEs: during the entire study period (Days 0-30).

Adverse event reporting additional description:

As there were no SAEs reported before protocol amendment 2, the number of subjects at risk for each reported SAE was the total number of subjects enrolled after the protocol amendment. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	GSK217744 Group 1
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Reporting group description:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation A vaccine in the primary study and a booster dose of either GSK217744 formulation A vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Reporting group title	GSK217744 Group 2
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Reporting group description:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the GSK217744 formulation B vaccine in the primary study and a booster dose of either GSK217744 formulation B vaccine (for subjects vaccinated before Protocol Amendment 2) or Infanrix hexa™ vaccine (for subjects vaccinated after Protocol Amendment 2) in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™/GSK217744 and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Reporting group title	Infanrix hexa Group
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Reporting group description:

Subjects aged between and including 12 and 15 months at the time of booster vaccination who received the Infanrix hexa™ vaccine in the primary study and a booster dose of Infanrix hexa™ in this study, coadministered with a booster dose of Prevenar 13®. The Infanrix hexa™ and Prevenar 13® vaccines were administered intramuscularly into the right and left sides of the thigh, respectively.

Serious adverse events	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 188 (0.53%)	1 / 187 (0.53%)	0 / 282 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Pneumonia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 188 (0.53%)	1 / 187 (0.53%)	0 / 282 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 188 (0.00%)	1 / 187 (0.53%)	0 / 282 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	GSK217744 Group 1	GSK217744 Group 2	Infanrix hexa Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	188 / 188 (100.00%)	187 / 187 (100.00%)	282 / 282 (100.00%)
General disorders and administration site conditions			
Pain (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 188 (27.13%)	57 / 187 (30.48%)	98 / 282 (34.75%)
occurrences (all)	51	57	98
Redness (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 188 (12.77%)	26 / 187 (13.90%)	73 / 282 (25.89%)
occurrences (all)	24	26	73
Swelling (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 188 (15.43%)	28 / 187 (14.97%)	58 / 282 (20.57%)
occurrences (all)	29	28	58
Drowsiness (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			

subjects affected / exposed	30 / 188 (15.96%)	35 / 187 (18.72%)	67 / 282 (23.76%)
occurrences (all)	30	35	67
Irritability/fussiness (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 188 (19.68%)	47 / 187 (25.13%)	102 / 282 (36.17%)
occurrences (all)	37	47	102
Loss of appetite (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 188 (14.36%)	28 / 187 (14.97%)	58 / 282 (20.57%)
occurrences (all)	27	28	58
Fever (Symptom reported in subjects enrolled after protocol amendment 2.)			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 188 (19.68%)	40 / 187 (21.39%)	83 / 282 (29.43%)
occurrences (all)	37	40	83
Diarrhoea (AE reported in subjects enrolled before protocol amendment 2.)			
subjects affected / exposed	5 / 188 (2.66%)	6 / 187 (3.21%)	4 / 282 (1.42%)
occurrences (all)	5	6	4
Injection site induration (AE reported in subjects enrolled before protocol amendment 2)			
subjects affected / exposed	7 / 188 (3.72%)	3 / 187 (1.60%)	5 / 282 (1.77%)
occurrences (all)	7	3	5
Pyrexia (AE reported in subjects enrolled before protocol amendment 2)			
subjects affected / exposed	4 / 188 (2.13%)	5 / 187 (2.67%)	5 / 282 (1.77%)
occurrences (all)	4	5	5
Pain (Symptom reported in subjects enrolled before protocol amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	56 / 188 (29.79%)	67 / 187 (35.83%)	63 / 282 (22.34%)
occurrences (all)	56	67	63
Redness (Symptom reported in subjects enrolled before protocol			

amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	55 / 188 (29.26%)	56 / 187 (29.95%)	59 / 282 (20.92%)
occurrences (all)	55	56	59
Swelling (Symptom reported in subjects enrolled before protocol amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	45 / 188 (23.94%)	43 / 187 (22.99%)	48 / 282 (17.02%)
occurrences (all)	45	43	48
Drowsiness (Symptom reported in subjects enrolled before protocol amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 188 (28.72%)	47 / 187 (25.13%)	47 / 282 (16.67%)
occurrences (all)	54	47	47
Irritability/fussiness (Symptom reported in subjects enrolled before protocol amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	69 / 188 (36.70%)	73 / 187 (39.04%)	74 / 282 (26.24%)
occurrences (all)	69	73	74
Loss of appetite (Symptom reported in subjects enrolled before protocol amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 188 (22.87%)	45 / 187 (24.06%)	46 / 282 (16.31%)
occurrences (all)	43	45	46
Fever (Symptom reported in subjects enrolled before protocol amendment 2)			
alternative assessment type: Systematic			
subjects affected / exposed	42 / 188 (22.34%)	41 / 187 (21.93%)	37 / 282 (13.12%)
occurrences (all)	42	41	37
Eye disorders			
Conjunctivitis (AE reported in subjects enrolled before protocol amendment 2.)			
subjects affected / exposed	3 / 188 (1.60%)	0 / 187 (0.00%)	7 / 282 (2.48%)
occurrences (all)	3	0	7
Infections and infestations			

Nasopharyngitis (AE reported in subjects enrolled after protocol amendment 2)			
subjects affected / exposed	9 / 188 (4.79%)	11 / 187 (5.88%)	10 / 282 (3.55%)
occurrences (all)	9	11	10
Otitis media (AE reported in subjects enrolled before protocol amendment 2)			
subjects affected / exposed	6 / 188 (3.19%)	11 / 187 (5.88%)	11 / 282 (3.90%)
occurrences (all)	6	11	11
Upper respiratory tract infection (AE reported in subjects enrolled before protocol amendment 2)			
subjects affected / exposed	6 / 188 (3.19%)	7 / 187 (3.74%)	9 / 282 (3.19%)
occurrences (all)	6	7	9
Nasopharyngitis (AE reported in subjects enrolled before protocol amendment 2)			
subjects affected / exposed	4 / 188 (2.13%)	2 / 187 (1.07%)	5 / 282 (1.77%)
occurrences (all)	4	2	5
Gastroenteritis (AE reported in subjects enrolled before protocol amendment 2)			
subjects affected / exposed	2 / 188 (1.06%)	2 / 187 (1.07%)	5 / 282 (1.77%)
occurrences (all)	2	2	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2011	<ol style="list-style-type: none">1. At the discretion of GSK Biologicals, pneumococcal testing may be done at a GSK Biologicals laboratory or the World Health Organisation (WHO) reference laboratory. Since the 22F-inhibition ELISA assay used at the WHO reference laboratory has a different assay cut-off, different thresholds are mentioned in the statistical analysis description. The threshold for the 22F-inhibition non-GSK ELISA assay performed at the WHO reference laboratory is 0.35 µg/ml.2. In order to simplify study management activities, the subjects will be given new treatment numbers in the present booster study.3. Exploratory statistical comparisons will be based on 97.5% CI instead of 95% to be aligned with the study objective criteria.
12 April 2012	<ol style="list-style-type: none">1. Due to the increased incidence of fever observed with the new formulations of the DTPa-HBV-IPV/Hib vaccine in the primary vaccination study 113948 (DTPa-HBV-IPV-124), all subjects yet to receive a booster dose in the present study will be administered the licensed formulation of Infanrix hexa.2. Because the safety and immunogenicity of commercial vaccines administered after Formulation A or Formulation B is unknown, this study will continue to ensure the safety of the subjects and adequate immune responses to the booster dose of Infanrix hexa.3. SBIR will be used to allocate new treatment numbers corresponding to Infanrix hexa vaccine to all newly enrolled subjects after amendment 2.4. After amendment 2, all subjects will receive Infanrix hexa. Accordingly less than half of the subjects can contribute to the initial study objectives leading to a study power lower than 50%. For this reason, separate analyses of the cohort enrolled pre and post amendment will be performed. These analyses will be descriptive without study group comparisons.
15 May 2012	At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported